



Perspective Article

Summary - Imaging of bones and joints

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Accelerating advances in biomedical imaging technologies is providing unprecedented opportunities to probe into the biological processes underlying human health and disease in ever more increasing detail, both at anatomical and functional level. Also, research in the imaging field is becoming more and more interdisciplinary. Importantly, there is a growing interdependence or interplay between basic biomedical/biological research, clinical medicine and drug design and development. Basic research has led to the development of technologies that have been successfully integrated into clinical medicine. As an example, the basic research in the field of nuclear magnetic resonance evolved into MRI which revolutionized clinical medicine. In other situations, it may be an unmet clinical need that stimulates basic research. For example, the prevailing view in clinical practice that the low bone mass is the sole determinant of osteoporotic fracture is somewhat limited in scope, because bone mineral density as measured by dual-energy X-ray absorptiometry (DXA) can not reliably predict fracture risk or its therapeutic reduction in osteoporotic women. The limitation of this one-dimensional view of osteoporosis has stimulated basic research leading to the development of imaging technologies including micro-computed tomography to measure bone quality, such as bone architecture and bone material properties, which are also important risk factors for osteoporotic fractures. The talks in this session fell into one or more of the three categories – basic biomedical/biological research, clinical medicine, and drug development. The bridging the knowledge and developments in the three areas remain a challenge.

Thomas Dufresne ("Novel 3-D image analysis and micro-CT applications in musculoskeletal research") described the application of micro-computed tomography for pharmaceutical development for osteoporosis and osteoarthritis. He

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highlighted the critical role that image analysis plays for successful implementation of any imaging modality. Through the development of automated image analysis algorithms (for example, 3-D automated algorithm to delineate cortical and trabecular regions in iliac crest samples, or automated separation of cartilage and subchondral bone in arthritic joints), Dufresne demonstrated that 3-D micro-CT technology can be routinely adapted into research in drug development where high throughput is essential.

The talk by **Charles Peterfy** ("Structural characterization of rheumatoid arthritis by MRI: Applications in clinical research and in clinical practice") showed that MRI has better sensitivity than conventional radiological methods to identify early pre-erosive phenotypes in patients with rheumatoid arthritis (RA). Much of these developments were stimulated by a shift in therapeutic strategy towards early treatment with structure-modifying therapies before the onset of erosive joint damage. MRI's ability to detect early changes may prove cost effective by reducing the time and cost of clinical trials and development of therapy.

Dan Gazit ("Imaging using osteocalcin-luciferase") described a cooled charged coupled device (CCCD) camera, a molecular imaging system to monitor luciferase expression regulated by an hOC (osteocalcin) promoter. Quantitative real-time monitoring of bioluminescence was used to track bone-specific gene expression *in vitro* and *in vivo* during bone development and regeneration.

In his talk ("Multi-modality imaging of musculoskeletal disease in small animals"), **Michael Thornton** described several emerging *in vivo* techniques (micro-CT, MR, SPECT, PET, dynamic-CT, and deep-tissue optical imaging) that are potentially applicable to study anatomy, physiology and function in small animal models. Of particular interest to the musculoskeletal research were the novel applications of dynamic-CT to probe blood flow, tissue permeability and perfusion in bone and *in vivo* fluorescence imaging of osteoblastic activity.

Martha Gray ("Molecular and functional imaging of articular cartilage") discussed the functional paradigm that the articular cartilage in osteoarthritis is under load and that any imaging method needs to take this into account. Changes in the cartilage molecular matrix can impair the functional integrity of the joint. Gray described elaborately

how novel MRI techniques can be used to non-invasively examine the changes of the composition and architecture of the macromolecules (GAG, collagen etc.) that are involved in cartilage and thus functional impairment. Techniques like delayed gadolinium-enhanced MRI of the cartilage (dGEMRIC) can be used in clinical settings to monitor therapeutic efficacy and disease progression.

Carol Muehleman ("Yes, you can see the cartilage with X-rays: Diffraction-enhanced imaging of cartilage and bone") described a novel radiographic imaging method that allows us to visualize the articular cartilage in disarticulated and intact joints. In diffraction-enhanced imaging (DEI), a monochromatic parallel X-ray beam (currently from a syn-

chrotron source) is passed through an object and a crystal analyzer placed between the object and the detector modulates the intensity according to the angular deviations of the X-rays through the object, thus producing high resolution, high-contrast image. Muehleman suggested that the imaging method is not limited to radiation from a synchrotron source, and has the potential for use in research and clinical settings without requiring excessive exposure to X-rays.

In closing, the session on imaging of bones and joints was a success, primarily due to the fact that it responded to the growing desire of the musculoskeletal community to embrace imaging in its research setting. The conference has brought to light many potentials and challenges as well.